

CLAIMS

1. A method of decreasing body weight in a patient, said method comprising administering a
5 therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.

2. A method of claim 1, wherein said method comprises administering a therapeutically effective amount of a somatostatin agonist to said patient.

10 3. A method of claim 2, wherein said somatostatin agonist is a somatostatin type-2 receptor agonist.

4. A method of claim 2, wherein said somatostatin agonist is a somatostatin type-5 receptor agonist.

15 5. A method of claim 3, wherein said somatostatin type-2 receptor agonist has a K_i of less than 2 nM for the somatostatin type-2 receptor.

6. A method of claim 4, wherein said somatostatin type-5 receptor agonist has a K_i of less than 2 nM for the somatostatin type-5 receptor.

20 7. A method of claim 2, wherein said somatostatin agonist is a somatostatin type-2 receptor selective agonist.

25 8. A method of claim 2, wherein said somatostatin agonist is a somatostatin type-5 receptor selective agonist.

9. A method of claim 7, wherein said somatostatin type-2 receptor selective agonist has a K_i for the somatostatin type-2 receptor that is at least 10 times less than the K_i for the somatostatin type-1, type-3,
30 type-4, and type-5 receptors.

10. A method of claim 8, wherein said
somatostatin type-5 receptor selective agonist has a K_i
for the somatostatin type-5 receptor that is at least 10
times less than the K_i for the somatostatin type-1, type-
5 2, type-3, and type-4 receptors.

11. A method of decreasing body weight in a
patient, said method comprising administering a
therapeutically effective amount of H-Cys-Phe-Phe-D-Trp-
Lys-Thr-Phe-Cys-NH₂, wherein a disulfide bond exists
10 between the free thiols of two Cys residues.

12. A method of claim 1, wherein said patient is
an non-insulin-dependent diabetic human..

13. A method of claim 2, wherein said patient is
an non-insulin-dependent diabetic human.

15 14. A method of claim 3, wherein said patient is
an non-insulin-dependent diabetic human.

15. A method of claim 4, wherein said patient is
an non-insulin-dependent diabetic human.

20 16. A method of claim 5, wherein said patient is
an non-insulin-dependent diabetic human.

17. A method of claim 6, wherein said patient is
an non-insulin-dependent diabetic human.

18. A method of claim 7, wherein said patient is
an non-insulin-dependent diabetic human.

25 19. A method of claim 8, wherein said patient is
an non-insulin-dependent diabetic human.

20. A method of claim 9, wherein said patient is
an non-insulin-dependent diabetic human.

30 21. A method of claim 10, wherein said patient is
an non-insulin-dependent diabetic human.

22. A method of claim 11, wherein said patient is an non-insulin-dependent diabetic human.

Just 23. A method according to claim 1 wherein the somatostatin agonist is

- 5 H-D- β -Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys- β -Nal-NH₂,
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys- β -Nal-NH₂,
- H-D- β -Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂,
- 10 H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂,
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH,
- H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH,
- H-Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH,
- H-Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH,
- 15 H-Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH,
- H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol
- H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
- H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- 20 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂,
- H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
- Ac-D-Phe-Lys'-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂ (an amide bridge formed between Lys' and Asp),
- 25 Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
- 30 Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

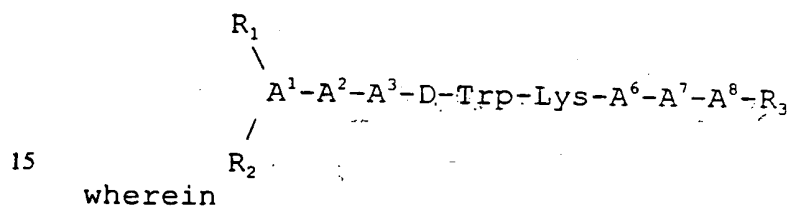
- Ac-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
 Ac-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂,
 Ac-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt,
 Ac-L-hArg (CH₂-CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
 5 Ac-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys (Me) -Thr-Cys-Thr-
 NH₂,
 Ac-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys (Me) -Thr-Cys-Thr-
 NHEt,
 Ac-hArg (CH₃, hexyl) -Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
 10 H-hArg (hexyl)₂ -Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
 Ac-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt,
 Ac-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂,
 Propionyl-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys (iPr) -Thr-Cys-
 Thr-NH₂,
 15 Ac-D-β-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg (Et)₂-
 NH₂,
 Ac-D-Lys (iPr) -Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
 Ac-D-hArg (CH₂CF₃)₂-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-
 Thr-Cys-Thr-NH₂,
 20 Ac-D-hArg (CH₂CF₃)₂-D-hArg (CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-
 Thr-Cys-Phe-NH₂,
 Ac-D-hArg (Et)₂-D-hArg (Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-
 Thr-NH₂,
 Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-
 25 Cys-NH₂,
 H-Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
 H-Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH₂,
 H-Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH₂,
 H-Bmp-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂,
 30 H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,

- H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-β-Nal-NH₂,
H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
Ac-D-β-Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH₂,
5 H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂,
H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
10 H-D-Phe-Cys-β-Nal-D-Trp-Lys-Val-Cys-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH₂,
cyclo(Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe),
cyclo(Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe),
cyclo(Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe),
15 cyclo(N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe),
cyclo(Pro-Tyr-D-Trp-Lys-Thr-Phe),
cyclo(Pro-Phe-D-Trp-Lys-Thr-Phe),
cyclo(Pro-Phe-L-Trp-Lys-Thr-Phe),
cyclo(Pro-Phe-D-Trp(F)-Lys-Thr-Phe),
20 cyclo(Pro-Phe-Trp(F)-Lys-Thr-Phe),
cyclo(Pro-Phe-D-Trp-Lys-Ser-Phe),
cyclo(Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe),
cyclo(D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe),
cyclo(D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe),
25 cyclo(D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe),
cyclo(D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr),
cyclo(Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe),
cyclo(Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe),
cyclo(N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe),

- cyclo(N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe),
 cyclo(Pro-Tyr-D-Trp-4-Amphe-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-4-Amphe-Thr-Phe),
 cyclo(N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe),
 5 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba),
 cyclo(Asn-Phe-D-Trp-Lys-Thr-Phe),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-β-Ala),
 10 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH,
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Gly),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly),
 15 cyclo(Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp(NO₂)-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba),
 20 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-
 OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-
 OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-
 25 OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-
 Cys)-OH,
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba),
 30 cyclo(Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba),

cyclo(Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-(CH₂)₃-CO),
 cyclo(Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 5 H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂,
 H-Cys-Phe-Phe-D-Trp-Lys-Ser-Phe-Cys-NH₂,
 H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH₂ or
 H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH₂.

24. A method according to claim 1 wherein the
 10 somatostatin agonist is



A¹ is a D- or L- isomer of Ala, Leu, Ile, Val,
 Nle, Thr, Ser, β-Nal, β-Pal, Trp, Phe, 2,4-dichloro-Phe,
 pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH₃,
 20 Cl, Br, F, OH, OCH₃ or NO₂;

A² is Ala, Leu, Ile, Val, Nle, Phe, β-Nal,
 pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-
 Phe, or p-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or
 NO₂;

25 A³ is pyridyl-Ala, Trp, Phe, β-Nal, 2,4-dichloro-
 Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is
 CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

A⁶ is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

A⁷ is Ala, Leu, Ile, Val, Nle, Phe, β-Nal,
 30 pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-
 Phe, or p-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or
 NO₂;

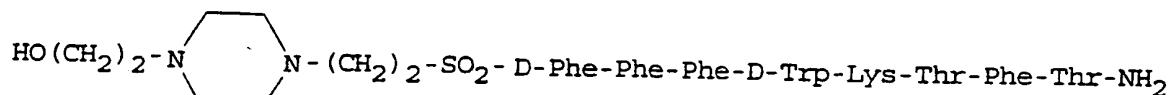
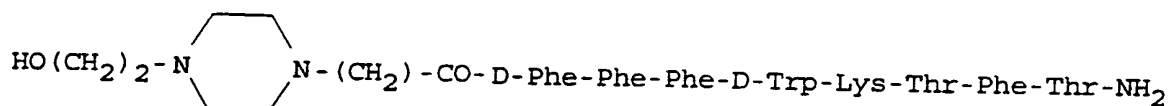
A⁸ is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, p-X-Phe, or o-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

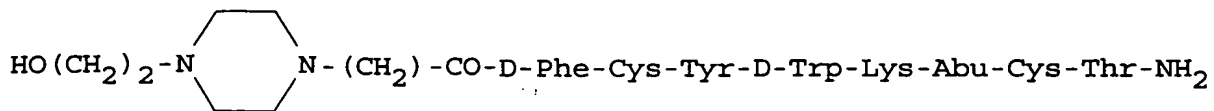
each R₁ and R₂, independently, is H, lower acyl or lower alkyl; and R₃ is OH or NH₂; provided that at least one of A¹ and A⁸ and one of A² and A⁷ must be an aromatic amino acid; and further provided that A¹, A², A⁷ and A⁸ cannot all be aromatic amino acids.

25. A method according to claim 24 wherein the linear somatostatin agonist is

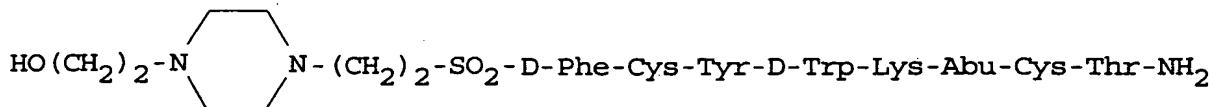
H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂,
 H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂,
 H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂ or
 H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala- β -D-Nal-NH₂.

26. A method according to claim 1 wherein the somatostatin agonist is





or



5

27. A method according to claim 1 wherein said patient is obese.

10 28. A method according to claim 3 wherein said patient is obese.

29. A method according to claim 4 wherein said patient is obese.

15 30. A method according to claim 7 wherein said patient is obese.

31. A method according to claim 8 wherein said patient is obese.

32. A method according to claim 11 wherein said patient is obese.

20 33. A pharmaceutical or cosmetic composition comprising a therapeutically or cosmetically effective amount of somatostatin; or a somatostatin agonist; or H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂ wherein a disulfide bond exists between the free thiols of the two
25 Cys residues.

34. A pharmaceutical composition as claimed in claim 33 having the features identified in any one of claims 3 to 10 and 23 to 26.

11 2007.99

35

35. Use of a somatostatin, or a somatostatin agonist; or H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂ wherein a disulfide bond exists between the free thiols of the two Cys residues, in the formulation of a
5 pharmaceutical or cosmetic composition for use in reducing excessive body weight in a human or mammalian animal.

36. Use of a somatostatin, or a somatostatin agonist according to claim 35, wherein said somatostatin
10 or somatostatin agonist has the relevant features identified in any one of claims 3 to 10 and 23 to 26.

37. A pharmaceutical composition substantially as hereinbefore described with reference to the Examples.

AMENDED SHEET